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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/732,782	12/10/2003	Stephen Hsu	275.0007 0101	6883

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EXAMINER	
PHAM, AUDREY S	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/732,782	HSU ET AL.	
	Examiner	Art Unit	
	Audrey S. Pham	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-35 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-35 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Re: Hsu *et al.*

Claims 1-35 are pending.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-6, drawn to a method of determining if cancer cells are resistant to an agent comprising determining the p57/KIP2 level in the cancer cells prior to contact with the agent contacting the cancer cells with the agent, determining the p57/KIP2 level by detecting the p57/KIP2 protein, classified in class 435, subclass 7.1.

II. Claims 1-5, 7, drawn to a method of determining if cancer cells are resistant to an agent comprising determining the p57/KIP2 level in the cancer cells prior to contact with the agent contacting the cancer cells with the agent, determining the p57/KIP2 level by detecting the mRNA encoding p57/KIP2, classified in class 435, subclass 6.

III. Claims 8-9, as specifically drawn to a method of determining if cancer cells are "sensitive" to an agent comprising determining the p57/KIP "protein" levels, classified in class 435, subclass 7.1

IV. Claims 8-9, as specifically to a method of determining if cancer cells are "sensitive" to an agent comprising determining the p57/KIP "nucleic acid" levels, classified in class 435, subclass 6.

V. Claims 10-11, drawn to a method of determining the therapeutic effectiveness of an agent comprising contacting cells with an agent determining the p57/KIP2 levels and comparing the normal cells with the cancer cells, classified in class 435, subclass 325.

VI. Claim 12, drawn to a method of optimizing the formulation of an agent for the treatment of a cancer, classified in class 435, subclass 4.

VII. Claims 13-18, 20, drawn to a method of preventing damage to non-cancerous cells in a subject undergoing cancer therapy comprising administering to the subject a polyphenolic composition under conditions effective to induce the expression of p57, classified in class 424, subclass 9.1.

VIII. Claims 13-18, 20, drawn to a method of preventing damage to non-cancerous cells in a subject undergoing cancer therapy comprising administering to the subject a polyphenolic composition under conditions effective to induce the expression of caspase-14, classified in class 424, subclass 184.1.

IX. Claims 13-18, 20, drawn to a method of preventing damage to non-cancerous cells in a subject undergoing cancer therapy comprising administering to the subject a polyphenolic composition under conditions effective to induce the expression of both p57 and caspase-14, classified in class 424, subclass 184.1.

X. Claim 19, drawn to a method of enhancing effectiveness of a cancer therapy in a subject undergoing cancer therapy comprising administering to the subject a polyphenolic composition under conditions effective to induce caspase 3-dependent apoptosis in cancer cells, classified in class 424, subclass 9.2.

XI. Claims 21-22, drawn to a method of treating a skin condition comprising contacting the skin with a polyphenolic composition under conditions effective to induce caspse-14 expression in keratinocytes, classified in class 424, subclass 9.8.

XII. Claim 23, drawn to a method of treating precancerous oral lesion comprising contacting the precancerous oral lesion with a polyphenolic composition under conditions effective to induce p57 expression in normal epithelial cells and induce caspase-3-dependent apoptosis in precancerous and cancerous epithelial cells, classified in class 424, subclass 9.7.

XIII. Claims 24-31, 33, an *in vitro* method for the identification of an agent that possesses both a cytotoxic effect on tumor cells and a protective effect on normal cells, wherein survival of normal cells is determined by detecting the induction of p57 protein, classified in class 435, subclass 4.

XIV. Claims 24-30, 32-33, an *in vitro* method for the identification of an agent that possesses both a cytotoxic effect on tumor cells and a protective effect on normal cells, wherein survival of normal cells is determined by detecting the induction of mRNA encoding the p57 protein, classified in class 435, subclass 6.

XV. Claim 34, drawn to an agent that possesses both a cytotoxic effect on tumor cells and a protective effect on normal cells, classified in class 536, subclass 24.5.

XVI. Claim 35, drawn to a kit for the identification of an agent that possesses both a cytotoxic effect on tumor cells and a protective effect on normal cells, classified in class 435, subclass 810.

The inventions are distinct, each from the other for the following reasons:

The inventions of groups XV-XVI and the methods of groups I-XIV are related as products and processes of use. The inventions can be shown to be distinct if one or both of the following can be shown: (i) the process for using the product as claimed can be practiced with another materially different product or (ii) the product as claimed can be used in a materially different process of using that product [see *MPEP* § 806.05(h)]. In the instant

case, the agent or kit, as claimed, can be used in a materially different process such as in methods of developing said agent or said kit, methods of treatment of skin conditions or methods of identifying cancer cells.

The agent of group XV is related to the kit of group XVI by virtue of the fact that the kit has the utility of identifying the agent. However, the agent has utility for possessing cytotoxic effect on tumor cells and a protective effect on normal cells. Therefore, they are distinct inventions because the agent can be made by other and materially distinct processes, such as purification from a natural source. Furthermore, the kit can be used for processes other than the identifying the agent, such as in identifying other agents or in determining if cancer cells are resistant to an agent or in enhancing effectiveness of cancer therapy. Therefore, the kit and the agent are distinct products.

The inventions of Groups I-XIV are materially distinct methods, which differ at least in objectives, method steps and reagents. For example, Groups I-II are drawn to methods of determining if cancer cells are resistant to an agent, with an objective that differs from the other groups. Group III-IV are drawn to methods of determining if cancer cells are sensitive to an agent. Group V is drawn to a method of determining the therapeutic effectiveness of an agent. Group VI is drawn to a method of optimizing the formulation of an agent for the treatment of a cancer. Group VII-IX are drawn to methods of preventing damage to non-cancerous cells in a subject. Group X is drawn to enhancing effectiveness of a cancer therapy in a subject undergoing cancer therapy. Group XI is drawn to a method of treating a skin condition. Group XII is drawn to a method of treating precancerous oral lesion and groups XIII-XIV are drawn to in vitro methods for the identification of an agent that possesses both cytotoxic effect and a protective effect. Furthermore, while some groups may have similar objectives, each groups employs chemically distinct reagents and method steps to achieve the objectives. For example, groups XIII and XIV are drawn to methods with similar objectives of identifying an agent that possesses both a cytotoxic effect on tumor cells and a protective effect on normal cells, group XIII identifies an agent by detecting induction of p57 protein while group XIV detects by induction of mRNA encoding the p57 protein. Likewise, groups VII-IX each employs chemically distinct reagents (p57, caspase-14 or both) to accomplish the objective of preventing damage to non-cancerous cells.

Searching all of the groups with all of the different reagents, steps or objectives would invoke a high burden of search.

These inventions are distinct for the reasons given above and they have acquired separate statuses in the art as shown by their different classifications. The search required for one group is not required for the other groups and vice versa. For these reasons, restriction for examination purposes as indicated is proper.

Applicant is reminded that the reply to this requirement to be completed must include an election of the invention to be examined even though the requirement be traversed (See 37 CFR 1.143).

Species Election

One or more of the above invention groups each contain multiple generic claims which include a plurality of alternatively usable substances or members. These alternative limitations are independent or distinct inventions such that they do not share a common utility or share a substantial structural feature disclosed as being essential to that utility. Because they are not so closely related, a search and examination of the entire claim cannot be made without undue burden. The members of the alternative groupings are described in the following:

Group I (Claims 2-3, 5) is generic to a plurality of disclosed patentably distinct species comprising the following epithelial cell lines: oral squamous carcinoma, metastatic oral carcinoma, and breast epithelial carcinoma.

The epithelial cell lines of the above species represent separate and distinct products that differ at least in etiology, pathology, and mechanisms. As such, each species would require different searches and the consideration of different patentability issues.

Groups VII-IX (Claims 14-15) are generic to a plurality of disclosed patentably distinct species comprising the following polyphenolic compositions: polyphenol (GTPP), (-)-

epicatechin (EC), (-)-epigallocatechin (EGC), (-) epicatechin-3-gallate (ECG), and (-)-epigallocatechin-3-gallate (EGCG).

The polyphenolic compositions of the above species represent separate and distinct molecules with different structures, chemicals, and functions such that one species could not be interchanged with the other. As such, each species would require different searches and the consideration of different patentability issues.

Additionally, Group XI (Claim 22) is generic to a plurality of disclosed patentably distinct species comprising the following skin conditions: psoriasis, aphthous ulcer, actinic keratosis, rosacea, wound, a burn, a skin condition associated with diabetes, a skin condition associated with aging, and a skin condition associated with altered keratinocyte differentiation.

Upon election of group I, VII-IX or XI, Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, Applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, Applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should Applicant traverse on the ground that the species are not patentably distinct, Applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either

instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Rejoining Claims

NOTE:

The Examiner has required restriction between product and process claims. Where Applicant elects claim(s) directed to a product and the product claim(s) is/are subsequently found allowable, the withdrawn process claim(s) that depend(s) from or otherwise include all the limitations of the allowable product claim(s) will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if an amendment is presented prior to a final rejection or allowance, whichever is earlier. Amendment submitted after final rejection is governed by 37 CFR 1.116; amendment submitted after allowance is governed by 37 CFR 1.312.

In the event of a rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claim(s) and process claim(s) may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the withdrawn process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Inventorship Amendment

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended to be in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request, as set forth in 37 CFR 1.48(b), and by a processing fee, as set forth in 37 CFR 1.17(i).

Contact Information

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Audrey S. Pham whose telephone number is (571) 272-3323. The Examiner can normally be reached during the hours of 8:30 AM - 5:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Jeffrey Siew, can be reached during business hours at the telephone number: (571) 272-0787. The fax number for the organization, where this application or proceeding is assigned, is (571) 273-8300.

Information REGARDING the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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